AMR Biosurveillance System in the Italian Region of Veneto

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Conflict of Interest

Arianna Cocchiglia, R&D manager
Lara Tramontan, Data manager

Have no real or apparent conflicts of interest to report.
Agenda

• **Who we are**: Arsenàl.IT and Veneto Region
• Background: the AMR (Antimicrobial resistance) threat and the need of a surveillance system
• Our ecosystem: from “islands” to HIE
• Second usage of data: our automatic and real time updated surveillance system
• A happy end: a working AMR surveillance system
• Our learned lessons..
Describe how standardization, interoperability, sharing and engagement contribute to build a real time biosurveillance system

Illustrate the advantages of the adoption of an integrated common semantic in order to easily interpret and share findings about international public health issues as antimicrobial resistance

Explain that monitoring processes can be the foundation of a biosurveillance integrated system in which many structures collaborate to share information

Identify the true potential of health data standardization in the context of our globalized society: sharing information in order to unify procedures all across the world and to create a common heritage, maintaining reliability in each level

Recognize how existing information can find a second usage, shifting from the singular identity to a global vision and considering data in their totality
Arsenàl.IT - Who we are

50+ people

32 yr average age

80% women
Where we are

Venice

about 5 million people
The Veneto Region

Administrative Framework

- 1 regional authority
  - 7 provinces (counties)
    - 575 municipalities

Healthcare System

- 1 regional public health system
  - 9 local health authorities (LHAs)
  - 2 hospital trusts (HTs)
  - 1 oncology research center
The AMR phenomenon

Antimicrobials are essential for infection treatments.

**Antimicrobial resistance (AMR)** is the ability of a microbe to resist the effects of medication that once could successfully treat the microbe.

AMR is a natural phenomenon intensified by repeated exposure to antimicrobials treatments.

In the last decades, the **misuse and abuse** of these drugs accelerated this process. ➢ **carbapenems: a serious threat!!**

last treatment option for patients infected with resistant bacteria!
The AMR: a global & local threat

- **CDC:** “more than 2 million illnesses and *about 23,000 deaths* in the United States annually”
- **ECDC:** “*about 25,000 deaths* in Europe annually”

Italy: some of the highest levels of resistance in Europe!!

- a resistance to carbapenems of 33.5% (31-36 95%CI) vs an European average of 8.1% (8-8 95%CI) for *Klebsiella Pneumoniae* (2015)
- a resistance to third-generation cephalosporins of 30.1% (29-31 95%CI) vs an European average of 13.1% (13-13 95%CI) for *Escherichia Coli* (2015)
How to combat AMR

Some suggestions from CDC.

**FOUR STRATEGIES TO COMBAT ANTIBIOTIC-RESISTANCE**

1. Preventing Infections, Preventing the Spread of Resistance
2. Tracking
3. Improving Antibiotic Prescribing and Use, Aka “Stewardship”
4. Developing New Drugs and Diagnostics

Our direct ACTION!
Global vision (microbiology data from around the world) but still limited number of sending structures involved (47 reporting laboratories in Italy, only 2 belonging to Veneto Region)

Data reported frequently, but with still a delay of some months
Surveillance systems requirements

- **timely** provision of information (*resistance pattern may vary over time*)
- **wide** geographical **coverage** (*resistance pattern vary in location*)
- high **data completeness and reliability**
- available linked information about the patient’s attributes (e.g. age, gender, clinical condition)

➢ to inform decision making and action!
  ➢ public health: new policies and guidelines
  ➢ clinicians: right and prompt empirical treatments
Why an AMR surveillance system in Veneto?

- **Emergency needs**: e.g.
  - Veneto Region: death rate for septicemia is 16.5 per 100,000 inhabitants (2013-2016)
  - in 2017 and 2018 resistant Klebsiella pneumoniae caused many deaths
- **Italian’s National Institute of Health** launched a National AMR monitoring program: a network of labs located all over the territory has been required
- **Public health and clinicians needs**: they started to ask for an AMR surveillance system
In 2012, there were 23 different realities.

- 23 different LISs
- 23 different test code systems (total codes: 1,150)
- 23 different test results code systems (total codes: 15,168)
- each LIS with its own patient’s identifier
They started to get in touch..

Same roads and same rules, same STANDARD infrastructure..

➢ they started DOCUMENT SHARING

IHE XDS, XUA, BPPC
They started to talk..

Same SYNTAX, same STANDARD document..
They started to understand each other..

Same STANDARD LANGUAGE

KLEBSIELLA PNEUMONIAE

KLEBSIELLA PNEUMONIAE

LOINC®
HL7 ObservationInterpretation,
HL7 SpecimenType,
HL7 ObservationMethod
Veneto HIE System

Total numbers:
- ePrescriptions: 121,586,123
- eReferrals: 64,091,607
- Radiology reports: 2,417,812
- ER reports: 1,720,404
- Discharge letters: 559,084
- Outpatient visit reports: 493,224
- Operative reports: 276,167
- Lab reports: 6,507,119
  - 572,626 microbiological reports (on average 2,176/day)
    - for outpatients: 1650/day (76%)
    - for inpatients: 526/day (24%)
Secondary usage of data

Italian HIE systems have, by law, 3 purposes:
1. Care
2. Governance
3. Research

Trusted Third Party
(Veneto Region)

HIE system

Personal data

anonymized data

Secondary data usage

Quality
Public Health
Research
A standard secondary data usage infrastructure

- **Automatic** and **real time** data collection
- **Standard queries** to retrieve clinical documents of interest (either “push” and “pull” options)
- **ETL process** for extracting data from documents (thanks to standard document syntax and semantic)
- **automatic and real time anonymization** process
- **pseudonymization process** allowed -> **longitudinal analysis** and **linkage** of different kinds of data
The AMR surveillance infrastructure

Community
- ePrescription (e.g. antibiotics)
- eRefferal (e.g. antiobiogram prescription)

Hospital
- GP’s EHR (XDS Doc Source & Consumer)
- Hospital EHR (XDS Doc Source & Consumer)
- Laboratory (XDS Repository)
- LIS (XDS Doc Source)
- Lab report

Regional Information System
- ePrescriptions & eReferrals (XDS Repository)
- XDS Doc Registry

Anonymous real time updated DB
- ePrescriptions
- eReferrals
- Microbiology reports
- Discharge Letters...

Web-based tool for AMR monitoring

TTP (anonymization)
Our AMR surveillance system

**High data completeness:** LHAs are monitored every day about their data completeness (> 90%, otherwise they lose money!)

**Wide geographical coverage:** all LHAs in Veneto Region (except one which will be soon integrated), both for outpatient and inpatient care setting

Value of data made available thanks to an interactive & user friendly **web-based AMR monitoring tool**

**Real time** data availability

**High data reliability:** all LISs certified through a testing process (pre-production tests) and quality indicators monitored automatically every day (post-production assessment)

**Data linkage:** possibility to stratify the analysis for many patient’s demographic and clinical characteristics (e.g. age, gender, clinical condition)
The web-based AMR tool

The AMR tool is still in a **prototype version**.

It is composed of 3 dashboards:

- Bacteria isolation dashboard
- Bacterial resistance dashboard
- Antibiotic usage dashboard
Bacteria isolation dashboard

Many stratifications
Bacteria isolation dashboard

Select the LHA of interest: All
Select the type of patient (inpatient/outpatient): All
Select the sample to consider: All
Select how many microbes you want to visualize: 20
Select the age range of interest: start: 0, end: 100
Select the period of interest: from: 2018-10-01 to: 2019-01-31

Number of isolated bacteria: trend over time

KLEBSIELLA PNEUMONIAE: Some hypervirulent strains can cause severe invasive infections (often liver abscesses with bacteraemia and metastatic infections) also occurring in healthy subjects!
Bacteria isolation dashboard (sepsis)

Blood and cerebrospinal fluid (invasive isolates) > actual systemic infections!
Bacteria isolation dashboard (sepsis)

Real time infection monitoring

Number of isolated bacteria: trend over time
Bacteria isolation dashboard

Different geographical pattern
Bacteria isolation dashboard

Different age range

Pediatric population

Adult population
Bacterial resistance dashboard

Klebsiella pneumoniae: AMR profile (% of resistant isolated bacteria stratified by antibiotic type)

- All types of sample
- Age brand: 0-100 years old
- Both inpatient & outpatient care settings
- Period of analysis: 1 October 2018 - 31 December 2018
- Minimum number of isolates per antibiotic: 10

Antibiograms with carbapenems (imipenem, meropenem, ertapenem):

- Test results: 5309
- Isolates: 2062
- Patients: 1660
- R o I test results: 621 ->12% (11%-13% CI 95%)
- Isolates R or I to at least 1 carbapenem: 270 ->13% (12%-14% CI 95%)
- Patients with at least 1 R o I isolate: 184 -> 11% (9%-13% CI 95%)

Cephalosporins, 4th Generation

Cephalosporins, 3rd Generation

Carbapenems
Klebsiella pneumoniae: AMR profile (% of resistant isolated bacteria stratified by antibiotic type)

- Only BLOOD and CSF samples
- Age brand: 0-100 years old
- Both inpatient & outpatient care settings
- Period of analysis: 1 October 2018 - 31 December 2018
- Minimum number of isolates per antibiotic: 10

Antibiograms with carbapenems (imipenem, meropenem, ertapenem):
- Test results: 330
- Isolates: 139
- Patients: 94
- R or I test results: 14% (10%-18% CI 95%)
- Isolates R or I to at least 1 carbapenem: 15% (9%-21% CI 95%)
- Patients with at least 1 R or I isolate: 13% (6%-20% CI 95%)

< 33% of resistant bacteria to carbapenems reported by EARS-net

carbapenems
Bacterial resistance dashboard

Klebsiella pneumoniae: AMR profile (% of resistant isolated bacteria stratified by antibiotic type)

- Only BLOOD and CSF samples
- Age brand: 0-100 years old
- Both inpatient & outpatient care settings
- Period of analysis: 1 December 2017 - 31 December 2018
- Minimum number of isolates per antibiotic: 10

Antibiograms with carbapenems (imipenem, meropenem, ertapenem):
- Test results: 542
- Isolates: 223
- Patients: 159
- R out test results: 19% (16%-22% CI 95%)
- Isolates R or I to at least 1 carbapenem: 16% (13%-23% CI 95%)
- Patients with at least 1 R o I isolate: 16% (10%-22% CI 95%)

< 33% of resistant bacteria to carbapenems reported by EARS-net

carbapenems
Escherichia coli: AMR profile (% of resistant isolated bacteria stratified by antibiotic type)

- 20.2% of isolates R to aminoglycosides (tobramycin & gentamicin)
- 30.1% of isolates R to cephalosporins, 3rd Gen.

**Veneto Region**

- Only BLOOD and CSF samples
- Age brand: 0-100 years old
- Both inpatient & outpatient care settings
- Period of analysis: 1 October 2018 - 4 February 2019
- Minimum number of isolates per antibiotic: 30

**LHA a**

- Carbapenems

**LHA b**

- Carbapenems
Bacterial resistance dashboard

Escherichia coli: AMR profile (% of resistant isolated bacteria stratified by antibiotic type)

- Pediatric population (0-18)
- Adult population (>=65)

- All samples
- Both inpatient & outpatient care settings
- Period of analysis: 1 January 2018 - 4 February 2019
- Minimum number of isolates per antibiotic: 30
Antibiotic usage dashboard

Select LHA of interest

Select the type of practitioner

Select the class of antibiotics

Insert the age range of interest

Insert the period of interest (Prescription)
from: 2018-06-01 to: 2019-02-03

Select the period of interest (Dispensation)
from: 2018-06-01 to: 2019-02-03

Type of dispensed antibiotics (DDOs): analysis for 3rd and 5th ATC level

- FLU SEASON!
- CEPIALBINO
- AZITHROMICIN
- MACROLIDES, LINC.
- RIFAMICIN
- QUINOLINES
- CELIPROLOL

- FLU SEASON!
- CMPH: 3rd generation!
Antibiotic usage dashboard

Number of DDDs dispensed by antibiotic type: trend over time

Type of dispensed antibiotics (DDDs): analysis for 3rd and 5th ATC level

Real time data!

elderly people
The AMR tool is still in a **prototype version**, we are defining it in a working group with also clinicians, researchers and Regional public health officers.

The final users will be both clinicians (GPs and hospital doctors) and public health officers, moreover it will be made available for research.

This tool is aimed to:

- **support clinicians** as a Decision Support System for **empiric prescription**
- allow **public health officers** to **monitor** the AMR status in Veneto Region, in hospitals and in the community
- allow public health officers, **researchers** and clinicians to **define new and updated guidelines** for appropriate antibiotic prescription
- we will to integrate the patient’s AMR status in the Regional drug-drug interaction clinical support system
It was not an easy journey..

Main issue: **Resistance to change!!!**

**Adoption of new standards** (new vocabularies & new document structure) for laboratory staff: **a really hard task**

- A “mandatory” request to change is important (a change imposed from the top)

but not enough: **the real change come from the bottom**

- meetings have been organized to engage and motivate
- the advantages of standard have to be shown (precision, accuracy: e.g. only one LOINC® code convey many precise information: sample, method, metrics)
- laboratories staff was assisted by a specifically-developed system for translating codes
It was not an easy journey..

Some technical issues..

❖ Choice of public, international or at least national codifications, as much complete as possible
  ➢ a germ codification that meets the requested criteria was not found -> new codify is being created by the Italian national association of clinical microbiologists
  ➢ Some codes have been added to HL7 ObservationMethod and HL7 SpecimenType to include specific Veneto Region codes

❖ Laboratory and **microbiological CDA2 reports have a very complex structure!**
  ➢ High quality reached trough:
    i. Labeling process (pre-production tests)
    ii. Daily automatic evaluation of quality indicators (in production stage)
  ➢ Time consuming ETL process:
    i. a cloud solution & many parallel process can help!
Some keynotes for you..

The creation of a real time and evidence-based biosurveillance system is not a local, but a **Regional/National asset**.

The drivers:

- ★ Sharing
- ★ Standardization
- ★ Integration
- ★ Interoperability

But the change is not (only) a technical issue!

**Standardization does not reduce information, it can be an enrichment, because it encourages the sharing of the local knowledge and the learning between people.**
Questions

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